REMARKS

This application has been amended in a manner that is believed to place it in condition for allowance at the time of the next Official Action.

Claims 1-5 are pending in the present application. Claims 1-3 have been amended to more particularly point out and distinctly claim the present invention. New claims 4 and 5 have been added. Support for new claims 4 and 5 may be found in the original claims and generally throughout the specification.

In the outstanding Official Action, the specification was objected to for reciting "0/00". As suggested by the Examiner, this term has been deleted and replaced with the term "$^{0}/_{00}$".

The Official Action also suggested that the term "NMR-FINS" be changed to "NMR-SNIF" and that the complete name of the method be placed in the specification. Indeed, in the interest of advancing prosecution, the specification has been amended in this manner.

Applicants would like to thank Examiner Gakh for the suggestions as how to overcome these objections.

Claims 1-3 were objected to for allegedly not being written according to U.S. practice. Applicants believe that the present amendment obviates this objection.

In imposing the objection, the Official Action stated that the claims did not recite a preferred transitional phrase.

Claim 1 has been amended to recite the transitional phrase "comprising". Dependent claims 2 and 3 recite the transitional phrase "wherein". As a result, applicants believe that this objection has been obviated.

Claims 1-3 were rejected under 35 USC §103(a) as allegedly being unpatentable over any of MARTIN et al. (JACS, 1982), CAER et al., VALLET et al., HANNEGUELLE et al., MARTIN et al. (J. Agric. Food Chem., 1996) or JAMIN et al. This rejection is respectfully traversed.

Applicants believe that the cited publications, alone or in combination with each other, fail to disclose or suggest the claimed invention. The claimed invention relates to a process for analyzing a complex molecule in a sample relative to a reference or standard sample containing the same complex molecule. By practicing the claimed process, one can compare the degree of similarity between complex molecules and/or determine how a complex molecule has been produced. The process of the present invention comprises:

- cleaving the complex molecule to obtain analyzable molecular sub-entities,

- determining the isotopic profile of the molecular sub-entities via NMR to measure the specific positional isotopic content, and

- comparing the isotopic profile of the cleavage products with reference products.

In the process of the present invention, the cleavage step results in the production of an isotopic imprint, site by site, of at least one cleavage product from a selected isotope. The cleavage step generates sub-units obtained which are compatible with the intermediates of synthesis used in the production of the sample complex molecules.

Until the present invention, applicants believed that those in the field all proceeded in a similar manner to authenticate and/or determine the specificity of a complex molecule. Generally, one skilled in the art would proceed by:

- evaluating the quantity of an exogenic element that would be found in the complex molecule and which would constitute the marker for this molecule; or

- evaluating an arrangement of an isotopic marking of the complex molecules.

In each method, those skilled in the art sought to modify the complex molecule to identify the complex molecule.

The modification is needed because of the direct analysis of the complex molecule. For example, the SNIF-NMR method does not provide pertinent and useful information when analyzing complex molecules such as Viagra. This is due to the extent of overlap of signals corresponding to the different sub-entities.

The claimed invention is distinct because it provides a process which is able to avoid marking the complex molecule

analyzed. Instead of attempting to identify the complex molecule according to specificities introduced into the molecule, applicants believe it is more productive to look at the specificities of the process of production. These specificities may be either the number or the type of step to be used, or the original materials or intermediate products entering into the process to permit the production of the complex molecule. This is accomplished by recognizing that there is an isotopic specificity for one of the cleavage products of the complex molecule used as a reference. The isotopic specificity exhibits a unique characteristic detectable during analysis.

Upon reviewing the cited publications, applicants believe it is apparent that none of the cited publications, alone or in combination with each other, teach the claimed invention. MARTIN et al. (JACS, 1982) teach a method that is directed to accessing the deuterium content of a specific molecular site. MARTIN et al. (JACS, 1982) work with a variety of anethole samples in an effort to show that the method can be used to characterize and identity natural products from different origins.

CAER et al. is directed to the determination of site-specific carbon isotope ratios at natural abundance by carbon-13 NMR spectroscopy. The purpose of the article is to define methodologies that determine site-specific carbon isotope ratios, estimate the analytical potential of the method, and study

different kinds of organic molecules. However, the publication is limited to ethanols, acetic acids and vanillins from different botanical or synthetic origins.

VALLET et al. is directed to a combination of mass spectrometry and site-specific NMR isotope analyses in the characterization of amino acids. VALLET et al. use a combination of methods to show the isotopic parameters of glutamic acid, aspartic acid, alanine, proline and lysine.

The HANNEGUELLE publication is directed to the authentication of essential oils. In particular, HANNEGUELLE et al. are interested in linalool and linalyl acetate.

MARTIN et al. (J. Agric. Food Chem., 1996) utilize SNIF-NMR methods to analyze maple syrup. The publication studies the isotopic ratios obtained from maple syrup.

Thus, none of the publications disclose or suggest the claimed process for the analysis of a sample of a complex molecule relative to a reference batch of the same complex molecule so as to determine their degree of similarity and/or the nature of their process of production.

JAMIN et al. is directed to a multi-element and multi-site isotopic analysis of nicotine from tobacco leaves. However, nicotine was chemically degraded into nicotinic acid so that the intramolecular distribution of carbon and nitrogen isotopes could be studied. Moreover, JAMIN et al. do not discuss the extent to which nicotine may be analyzed directly by the SNIF-NMR method.

AS a result, applicant believe that JAMIN et al. fail to disclose or suggest the claimed invention.

As to the other publications, molecules are transformed chemically in derivatives to render them analyzable. For example, citric acid may be transformed into triethylacetate. However, this chemical transformation cannot be assimilated by cleavage. Conversely, the claimed process utilizes a cleavage step. By doing so, one does not lose fragments and one does not introduce a new manner or structure which results in unreliable results. Indeed, the cleavage products of the claimed invention allow for the selection of a product to be analyzed, and isotopes to be selected, and allow for a site to be chosen so that a reliable identification of the complex molecule can be made.

None of the publications suggest a cleavage step that leads to sub-units that are directly comparable to the intermediates of synthesis used, nor that the information obtained from the study of these sub-units and fragments can be used to determine how the complex molecules were synthesized. As a result, applicants believe that the proposed combination of the cited publications fails to disclose or suggest the claimed invention.

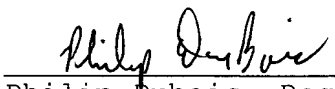
In view of the present amendment and the foregoing remarks, applicants believe that this application is now in condition for allowance, with claims 1-5, as presented.

Allowance and passage to issue on that basis are accordingly respectfully requested.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON



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